



## SEQUENCE LISTING

- <110> Institut de Recherches Cliniques de Montreal SEIDAH, Nabil CHRÉTIEN, Michel MARCINKIEWICZ, Mieczyslaw LAAKSONEN, Reijo DAVIGNON, Jean
- <120> MAMMALIAN SUBTILISIN/KEXIN ISOZYME SKI-1: A PROPROTEIN CONVERTASE WITH A UNIOUE CLEAVAGE SPECIFICITY
- <130> IRCM
- <140> PCT/CA99/01058
- <141> 1999-11-04
- <150> CA 2,249,648
- <151> 1998-11-04
- <160> 76
- <170> PatentIn Ver. 2.1
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一种 为

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- Ile Ala Ser Met Arg Glu Cys Gln Gly Phe Ala Pro Asp Ala Glu Leu 260 265 270
- His Ile Phe Arg Val Phe Thr Asn Asn Gln Val Ser Tyr Thr Ser Trp 275 280 285

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- Ile Val Asn Val Thr Ile Leu Asn Gly Met Gly Val Thr Gly Arg Ile 515 520 525
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- Ile Pro Ala Glu Gly Gly Gly Arg Ile Val Leu Tyr Gly Asp Ser Asn 835 840 845
- Cys Leu Asp Asp Ser His Arg Gln Lys Asp Cys Phe Trp Leu Leu Asp 850 855 860
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- His Ser Gly Asn Arg Gln Arg Pro Pro Ser Gly Ala Gly Leu Ala Pro 885 890 895
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Glu Val Glu Asn Trp Arg Ile Ile Pro Arg Asn Asn Pro Ser Ser Asp 85 90 95

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- Val Ala Gln Thr Leu Gln Ala Asp Val Leu Trp Gln Met Gly Tyr Thr 195 200 205
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- Val Ile Phe Ser Asp Trp Tyr Asn Thr Ser Val Met Arg Lys Val Lys
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- Met Tyr Tyr Ala Ser Gly Cys Ser Ile Ala Lys Phe Pro Glu Asp Gly 785 790 795 800
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- Ile Pro Ser Glu Gly Gly Gly Arg Ile Val Leu Tyr Gly Asp Ser Asn 835 840 845
- Cys Leu Asp Asp Ser His Arg Gln Lys Asp Cys Phe Trp Leu Leu Asp 850 855 860
- Ala Leu Leu Gln Tyr Thr Ser Tyr Gly Val Thr Pro Pro Ser Leu Ser 865 870 875 880
- His Ser Gly Asn Arg Gln Arg Pro Pro Ser Gly Ala Gly Leu Ala Pro 885 890 895
- Pro Glu Arg Met Glu Gly Asn His Leu His Arg Tyr Ser Lys Val Leu 900 905 910
- Glu Ala His Leu Gly Asp Pro Lys Pro Arg Pro Leu Pro Ala Cys Pro 915 920 925

His Leu Ser Trp Ala Lys Pro Gln Pro Leu Asn Glu Thr Ala Pro Ser 930 935 940

Asn Leu Trp Lys His Gln Lys Leu Leu Ser Ile Asp Leu Asp Lys Val 945 950 955 960

Val Leu Pro Asn Phe Arg Ser Asn Arg Pro Gln Val Arg Pro Leu Ser 965 970 975

Pro Gly Glu Ser Gly Ala Trp Asp Ile Pro Gly Gly Ile Met Pro Gly 980 985 990

Arg Tyr Asn Gln Glu Val Gly Gln Thr Ile Pro Val Phe Ala Phe Leu 995 1000 1005

Gly Ala Met Val Ala Leu Ala Phe Phe Val Val Gln Ile Ser Lys Ala 1010 1015 1020

Lys Ser Arg Pro Lys Arg Arg Pro Arg Ala Lys Arg Pro Gln Leu 025 1030 1035 1040

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atat	tcg	ctt o	gtgad		-	-	_						eu Le		c gtg eu Val	532
-	_		-		_			_		-	_	_	_	aag . Lys		580
		_	_	_		_		-						ttg Lėu		628
	_					-		_		-				gct Ala		676
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	_				_									atc Ile		868
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	-			_		-		_						aag Lys 155		964
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_		gtt gcc Val Ala	-		 _	-	-			_	1108
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2 2		cat ccc His Pro 225				_		_			1204
		cga acg Arg Thr		Asp A	 -						1252
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	tca Ser	_					_	-								3220
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ctg gac aag gtg gtg tta ccc aac ttt cga tcg aat cgc cct caa gtg 3412 Leu Asp Lys Val Val Leu Pro Asn Phe Arg Ser Asn Arg Pro Gln Val 960 965 970
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ttt gcc ttc ctg gga gcc atg gtg gtc ctg gcc ttc ttt gtg gta caa 3556 Phe Ala Phe Leu Gly Ala Met Val Val Leu Ala Phe Phe Val Val Gln 1005 1010 1015 1020
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cgc ccg cag ctc atg cag cag gtt cac ccg cca aag acc cct tcg gtg 3652 Arg Pro Gln Leu Met Gln Gln Val His Pro Pro Lys Thr Pro Ser Val 1040 1045 1050
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Ala Pro Cys Pro Gly Cys Ser His Leu Thr Leu Lys Val Glu Phe Ser 35 40 45

Ser Thr Val Val Glu Tyr Glu Tyr Ile Val Ala Phe Asn Gly Tyr Phe 50 55 60

Thr Ala Lys Ala Arg Asn Ser Phe Ile Ser Ser Ala Leu Lys Ser Ser 65 70 75 80

Glu Val Asp Asn Trp Arg Ile Ile Pro Arg Asn Asn Pro Ser Ser Asp 85 90 95

Tyr Pro Ser Asp Phe Glu Val Ile Gln Ile Lys Glu Lys Gln Lys Ala 100 105 110

Gly Leu Leu Thr Leu Glu Asp His Pro Asn Ile Lys Arg Val Thr Pro 115 120 125

Gln Arg Lys Val Phe Arg Ser Leu Lys Tyr Ala Glu Ser Asp Pro Thr 130 135 140

Val Pro Cys Asn Glu Thr Arg Trp Ser Gln Lys Trp Gln Ser Ser Arg 145 150 155 160

Pro Leu Arg Arg Ala Ser Leu Ser Leu Gly Ser Gly Phe Trp His Ala 165 170 175

Thr Gly Arg His Ser Ser Arg Arg Leu Leu Arg Ala Ile Pro Arg Gln
180 185 190

Val Ala Gln Thr Leu Gln Ala Asp Val Leu Trp Gln Met Gly Tyr Thr

195 200 205

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Ile	Ala	Ser	Met 260	Arg	Glu	Cys	Gln	Gly 265	Phe	Ala	Pro	Asp	Ala 270	Glu	Leu
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Phe	Leu 290	Asp	Ala	Phe	Asn	Tyr 295	Ala	Ile	Leu	Lys	Lys 300	Ile	Asp	Val	Leu -
Asn 305	Leu	Ser	·Ile	Gly	Gly 310	Pro	Asp	Phe	Met	Asp 315	His	Pro	Phe	Val	Asp 320
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Ser	Pro	Val	Val 420	Ala	Gly	Ala	Val	Thr 425	Leu	Leu	Val	Ser	Thr 430	Val	Gln
Lys	Arg	Glu 435	Leu	Val	Asn	Pro	Ala 440	Ser	Met	Lys	Gln	Ala 445	Leu	Ile	Ala

Ser Ala Arg Arg Leu Pro Gly Val Asn Met Phe Glu Gln Gly His Gly

450 455 . 460

Lys 465	Leu	Asp	Leu	Leu	Arg 470	Ala	Tyr	Gln	Ile	Leu 475	Asn	Ser	Tyr	Lys	Pro 480
Gln	Ala	Ser	Leu	Ser 485	Pro	Ser	Tyr	Ile	Asp 490	Leu	Thr	Glu	Cys	Pro 495	Туі
Met	Trp	Pro	Tyr 500	Cys	Ser	Gln	Pro	Ile 505	Tyr	Tyr	Gly	Gly	Met 510	Pro	Thi
Val	Val	Asn 515	Val	Thr	Ile	Leu	Asn 520	Gly	Met	Gly	Val	Thr 525	Gly	Arg	Ile
Val	Asp 530	Lys	Pro	Asp	Trp	Gln 535	Pro	Tyr	Leu	Pro	Gln 540	Asn	Gly	Asp	Asr
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Asp	Asn	Leu	Arg	Met 645	Lys	Asn	Asp	Pro	Leu 650	Asp	Trp	Asn	Gly	Asp 655	His
Ile	His	Thr	Asn 660	Phe	Arg	Asp	Met	Tyr 665	Gln	His	Leu	Arg	Ser 670	Met	Gl
Tyr	Phe	Val 675	Glu	Val	Leu	Gly	Ala 680	Pro	Phe	Thr	Cys	Phe 685	Asp	Ala	Sei
Gln	Tyr 690	Gly	Thr	Leu	Leu	Met 695	Val	Asp	Ser	Glu	Glu 700	Glu	Tyr	Phe	Pro

Glu Glu Ile Ala Lys Leu Arg Arg Asp Val Asp Asn Gly Leu Ser Leu

Val	Ile	Phe	Ser	Asp	Trp	Tyr	Asn	Thr	Ser	Val	Met	Arg	Lys	Val	Lys
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Ala Asn Ile Pro Ala Leu Asn Glu Leu Leu Ser Val Trp Asn Met Gly 755 760 765

Phe Ser Asp Gly Leu Tyr Glu Gly Glu Phe Thr Leu Ala Asn His Asp 770 775 780

Met Tyr Tyr Ala Ser Gly Cys Ser Ile Ala Lys Phe Pro Glu Asp Gly 785 790 795 800

Val Val Ile Thr Gln Thr Phe Lys Asp Gln Gly Leu Glu Val Leu Lys 805 810 815

Gln Glu Thr Ala Val Val Glu Asn Val Pro Ile Leu Gly Leu Tyr Gln 820 825 830

Ile Pro Ala Glu Gly Gly Arg Ile Val Leu Tyr Gly Asp Ser Asn 835 840 845

Cys Leu Asp Asp Ser His Arg Gln Lys Asp Cys Phe Trp Leu Leu Asp 850 855 860

Ala Leu Leu Gln Tyr Thr Ser Tyr Gly Val Thr Pro Pro Ser Leu Ser 865 870 875 880

His Ser Gly Asn Arg Gln Arg Pro Pro Ser Gly Ala Gly Ser Val Thr 885 890 895

Pro Glu Arg Met Glu Gly Asn His Leu His Arg Tyr Ser Lys Val Leu 900 905 910

Glu Ala His Leu Gly Asp Pro Lys Pro Arg Pro Leu Pro Ala Cys Pro 915 920 925

Arg Leu Ser Trp Ala Lys Pro Gln Pro Leu Asn Glu Thr Ala Pro Ser 930 935 940

Asn Leu Trp Lys His Gln Lys Leu Leu Ser Ile Asp Leu Asp Lys Val 945 950 955 960

Val Leu Pro Asn Phe Arg Ser Asn Arg Pro Gln Val Arg Pro Leu Ser

4-14 4-15 1- 4-14 1- 4-15 1- 4

ļ.

Pro Gly Glu Ser Gly Ala Trp Asp Ile Pro Gly Gly Ile Met Pro Gly 980 985 990

Arg Tyr Asn Gln Glu Val Gly Gln Thr Ile Pro Val Phe Ala Phe Leu 995 1000 1005

Gly Ala Met Val Val Leu Ala Phe Phe Val Val Gln Ile Asn Lys Ala 1010 1015 1020

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<223> Xaa represents any amino acid.

<220>

<221> MOD\_RES -

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<223> Xaa represents an alkyl or an aromatic hydrophobic amino acid.

<220>

<221> MOD\_RES

<222> (4)..(6)

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<220>

<221> MOD RES

<222> (7)

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Arg Xaa Xaa Xaa Xaa Xaa
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<223> Xaa represents Lys, Leu, Phe or Thr.
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<400> 23	
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20

agccctatta cctgaacctg

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12107 1101110	5 <b>4</b> p205					
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28

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<400> 36
ctcgagtgtc tgggcaacct ggcgcggg

<210> 37
<211> 14
<212> PRT
<213> Homo sapiens

<400> 37
Lys Ala Gly Ser Arg Gly Leu Thr Ser Leu Ala Asp Thr Phe
1 5 10
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<210> 38 <211> 27 <212> PRT <213> Homo sapiens

<400> 38
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1 5 10 15

Ser Val Leu Ser Phe Glu Ser Gly Ser Gly Gly  $20 \hspace{1cm} 25$ 

<210> 39 <211> 18 <212> PRT <213> Homo sapiens <400> 39

Trp His Ala Thr Gly Arg His Ser Ser Arg Arg Leu Leu Arg Ala Ile 1 5 10 15

Pro Arg

<210> 40 <211> 17 <212> PRT <213> Artificial Sequence <220>

<223> Description of Artificial Sequence: Peptide

<212> PRT

<213> Homo sapiens

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<210> 41
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Ser Arg Arg Leu Leu Arg Ala Leu Glu
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<211> 17
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<213> Homo sapiens
Trp Gln Ser Ser Arg Pro Leu Arg Arg Ala Ser Leu Ser Leu Gly Ser
                  5
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                                                          15
Gly
<210> 43
<211> 15
<212> PRT
<213> Homo sapiens
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Arg Ala Ile Pro Arg Gln Val Ala Gln Thr Leu Gln Ala Asp Val
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Pro Gln Arg Lys Val Phe Arg Ser Leu
<210> 45
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<212> PRT
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Pro Gln Arg Lys Val Phe Arg Ser Leu Lys Tyr Ala Glu Ser Asp
<210> 46
<211> 14
<212> PRT
<213> Artificial Sequence
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<223> Xaa represents 3-nitrotyrosine.
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<223> Xaa represents orthoaminobenzoic acid.
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<223> Xaa represent 3-nitrotyrosine.
<223> Description of Artificial Sequence: Peptide
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<210> 48
<211> 16
<212> PRT
<213> Homo sapiens
<400> 48
Lys Ala Gly Ser Arg Gly Leu Thr Ser Leu Ala Asp Thr Phe Glu His
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<210> 49
<211> 16
<212> PRT
<213> Rattus sp.
<400> 49
Lys Ala Gly Ser Arg Gly Leu Thr Thr Thr Ser Leu Ala Asp Thr Phe
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<210> 50
<211> 16
<212> PRT
<213> Homo sapiens
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<210> 51
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<212> PRT
<213> Homo sapiens
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Arg Lys Val Phe Arg Ser Leu Lys Tyr Ala Glu Ser Asp Pro Thr Val
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<210> 52
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<212> PRT
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<210> 53
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<213> Homo sapiens
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Val Thr Pro Gln Arg Lys Val Phe Arg Ser Leu Lys Lys Tyr Ala Glu
<210> 54
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Ser Gly Ser Gly Arg Ser Val Leu Ser Phe Glu Ser Gly Ser Gly Gly
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<210> 55
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<212> PRT
<213> Homo sapiens
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<210> 56
<211> 16
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<212> PRT
<213> Rattus sp.
<400> 56
Ala Ser Val Gly Arg Leu Ala Leu Ser Gln Glu Glu Pro Ala Pro Leu
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<210> 57
<211> 16
<212> PRT
<213> Homo sapiens
<400> 57
Arg Ile Ser Asp Arg Asp Tyr Met Gly Trp Met Asp Phe Gly Arg Arg
<210> 58
<211> 16
<212> PRT
<213> Rattus sp.
<400> 58
Asp Pro Arg Leu Arg Gln Phe Leu Gln Lys Ser Leu Ala Ala Thr
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<210> 59
<211> 16
<212> PRT
<213> Bovis sp.
<400> 59
Leu Leu Lys Glu Leu Gln Asp Leu Ala Leu Gln Gly Ala Lys Glu Arg
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<210> 60
<211> 16
<212> PRT
<213> Bovis sp.
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<210> 61
<211> 16
<212> PRT
<213> Bovis sp.
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<210> 62
<211> 16
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Ala Ala Met Asp Leu Glu Leu Gln Lys Ile Ala Glu Lys Phe Ser Gly
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<210> 63
<211> 16
<212> PRT
<213> Rattus sp.
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Lys Ser Ser Phe Thr Asn Val Thr Ser Pro Val Val Leu Thr Asn Tyr
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<210> 64
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<210> 65
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Leu Leu Arg Lys Lys Arg Thr Thr Ser Ala Glu Lys Asn Thr Cys Gln
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<212> PRT
<213> Homo sapiens
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Glu Glu Ile Ser Glu Val Lys Met Asp Ala Glu Phe Arg His Asp Ser
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Glu Glu Ile Ser Glu Val Asn Leu Asp Ala Glu Phe Arg His Asp Ser
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<210> 71
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Glu Phe Arg His Asp Ser Gly Tyr Glu Val His His Gln Lys Leu Val
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<210> 72
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<400> 72
Ser Ser Arg Arg Leu Leu Arg Ala Ile Glu
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<210> 73
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Ser Gly Ser Gly Arg Ser Val Leu Ser Phe Glu Ser
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<210> 74
<211> 14
<212> PRT
<213> Artificial Sequence
<220>
<221> MOD_RES
<222> (1)
<223> Xaa represents orthoaminobenzoic acid.
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<221> MOD RES
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<223> Xaa represents 3-nitrotyrosine.
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<210> 75
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<400> 75
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<210> 76
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<223> Xaa represents 3-nitrotyrosine.

<220>

<223> Description of Artificial Sequence: Peptide

<400> 76

Xaa Asn Gly Pro Lys Ala Gly Ser Arg Gly Leu Thr Ser Xaa Ala
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